SACRAMENTO MEDICAL FOUNDATION | Blood Centers

October 6, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket Number 98N-0581

Dear Sir:

These comments are pursuant to your recently published Rules and Proposed Rules entitled, **"Requirements for Testing Human Blood Donors for Evidence of Infection Due to Communicable Disease Agents and Requirements for Blood, Blood Components, and Blood Derivatives; Rules and Proposed Rules."** Overall, I think the proposal is appropriate. It is timely to revise the general biological product standards for infectious disease tests which are currently being performed on blood and plasma intended for transfusion, or further manufacture into transfusable plasma derivatives, as well as any testing incident to these, e.g., qualifying testing.

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On page 45341, it is proposed that autologous donations be tested for the same communicable disease agents as allogeneic units. While I support such testing, I do not see how this will reduce the risk of transmission of communicable diseases by untested units, since autologous donations with reactive tests can, and should, be returned to the intended donor/recipient. Further, it would appear to be a violation of the American Disabilities Act to interdict reactive autologous units from being drawn and transfused into the patient who provided them. While supplemental, additional, more specific testing of all donations that are repeatedly reactive by screening tests should be carried out, I do not believe these should be applied to screening test reactive autologous donations. These patients should be referred to their physicians, along with their reactive results, for confirmation, further evaluation and counseling.

On the same **page 45341, under II. Legal Authority,** it is clear that the FDA may make and enforce regulations under Section 361 of the PHS Act. Such regulations would also be enforceable in inspections of licensed establishments, and should also apply to registered ones. However, recommendations and guidelines are not regulations, and should not be enforced as such. Further, until such recommendations and guidelines become codified as regulations in the CFR, they should not be enforceable, unless accepted into the standard operating procedures of the establishment.

Again, on **page 45341**, and continuing over to **page 45341**, the requirement to test all human blood and blood components for communicable disease agents is to be applied to autologous units. In addition, such reactive units should be further tested with a supplemental, more specific test. While supplemental and specific tests should be applied to all allogeneic donations of blood, plasma, and component collections, this is not appropriate for autologous patient collections, where the screening tests should be done but, if reactive, the results should be provided to the patient's referring physician for further confirmation and follow-up. I do support provision of criteria for release or

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shipment of human blood or blood components prior to completion of testing in specified circumstances.

I am pleased to see **under Section A. Required Testing for Communicable Disease Agents, on page 45342,** that the FDA recognizes the potential of nucleic acid screening tests as replacements for some current methods of testing. I would certainly encourage the FDA to issue draft guidance and request open comment on nucleic acid testing in the near future, as noted. When the FDA recommends immediate implementation of "guidance" under its current good guidance practices (62 FR 8961, February 27, 1997), it should provide supporting data, as well as evidence for this necessity of protecting the public health. If there is not clear and substantial evidence of danger to the public health, then the FDA should not recommend immediate implementation of "guidance," but wait for comment.

On page 45343, under B. Affected Products, it is proposed, under Section 610.40 that there be uniform testing for both autologous and allogeneic donations, ***"thus significantly reducing any risk to the public health posed by the inadvertent improper use of potentially infectious products."*** While I support testing of autologous units for the same communicable diseases as allogeneic donations, the only way to prevent the inadvertent and improper use of some potentially infectious units would be to prevent release of those with reactive tests. Under the American Disabilities Act, and a recent Supreme Court decision on it, this would appear to be improper, unethical and illegal. Further, as noted later, on the same page, I believe it appropriate to apply the testing to each individual autologous donation, even if collected in a series, as well as all the units collected from dedicated apheresis donors, despite being intended for a single recipient. Regardless of test results, all autologous units should be labeled to identify them as not intended for allogeneic use (unless so qualified).

Page 45344, Section D. Further Testing, I support the agency's proposal to require that further testing by supplemental "confirmatory assays" be applied to samples which are repeatedly reactive, if they are drawn on allogeneic donors of blood and blood components. Similarly, this should apply to plasma collected from individuals, whether they are paid or volunteer, as well as any initial or qualifying testing on such individuals.

Under Section F. Release or Shipment Prior to Testing, I agree that medical emergencies may occur, which require shipment or release of untested or incompletely tested blood or blood components, so this should not be prohibited. However, any standard operating procedure spelling out the conditions for such emergency release should be present at the establishment and should not require prior approval from the FDA. If specific FDA approval had to be obtained, then, patients certainly could not wait for this, if they could not wait for completion of testing in a true emergency.

Under Section G. Restrictions on Shipment or Use, here it is proposed that testing would not apply to units intended for autologous use. This is, thus, inconsistent with the prior section. Why not just label all untested blood as "biohazard" if drawn from autologous patients? Further, it would be illegal in some states to label a unit from an autologous patient/donor which is found to be HIV-positive as such, without violating confidentiality.

Regarding **page 45345**, the FDA should permit the use of blood or blood components from a donor who is deferred as a result of his/her testing result, if the donor now can be re-entered. The donor re-entry algorithms have to be reasonable, based upon available science, and feasible for this to occur. The FDA should promptly update, e.g., the HIV re-entry algorithm, if data are available to do so, whether published or not.

On the same page 45345, Section I. Donor Deferral, it is not reasonable to defer donors with one repeatedly reactive test for HTLV I or II antibody, especially if the supplemental test is negative. A simple re-entry algorithm should be established which would permit such donors with negative, "confirmatory" tests to be re-entered at some time in the future when their test for the screening assay is non-reactive. Further, in the same section, I would agree that the FDA should permit donors testing repeatedly reactive for HTLV, types I and II, antibody, or anti-HBc, to serve as sources of plasma. Thus, I disagree with the agency's proposal to restrict such individuals with anti-HBc only to the preparation of Hepatitis B Immune Globulin. Such individuals should be permitted to provide source plasma for further manufacture of any plasma derivative.

On page 45347, the FDA uses the term "paid plasma donors" in contrast to volunteer blood donors. Since the former term is an oxymoron, it should be changed to "paid plasma sellers," or just sellers of blood components, as appropriate. Those exchanging their blood, blood components or plasma for money are not donors. Further, as noted later on the same page, the plasma industry should perform confirmatory testing on repeatedly reactive plasma or platelet units for HIV and HCV to notify properly and to inform these individuals of their results, whether performed on screening testing or on actual, collected units.

On page 45348, the approximate percentages and cost accounting for testing are specified for many of the assays currently performed. However, there is no cost accounting for HIV p24 antigen testing, and this should certainly be included. Further, the costs may differ considerably for allogeneic donors, as compared to autologous patients. The FDA should look further than Reference 9 for results of testing of allogeneic versus autologous donations. In this individual's experience, autologous patient/donors have much higher infectious disease rates even when compared to first-time, allogeneic donors. On the same page, it is noted that autologous units may be stored in the same freezers as allogeneic units. Actually, they would more likely be stored in refrigerators. In any case, whether labeled after testing, or not, autologous units (and even allogeneic units) may still pose a risk of transmitting infectious diseases despite non-reactive testing. A standard operating procedure should be put into place to minimize the chance of transfusion of autologous units to the wrong patient.

On page 45348, it is stated that ***"in 1994, 4.3% of all HCV infections were transfusion related."*** The reference should be provided for this number, which appears inordinately high for that year, especially compared to the ***"current rate of .02% to .05%."***

On page 45355, it is stated that donors with prior evidence of infection due to hepatitis B virus may give blood or blood components for preparation of Hepatitis B Immune Globulin, ***"provided their current donations test non-reactive when tested in***

accordance with Section 610.40(a), and the donor is otherwise determined to be suitable." Does this mean, for example, that a donor would, at that point, have to test non-reactive for anti-HBc? Certainly, I agree that ***"donors with a reactive serologic test for syphilis need not be deferred if found negative by an approved specific treponemal test (confirmatory test for syphilis)."*** Such individuals should be allowed to donate if their serologic test for syphilis is shown to be non-specific, or falsely positive.

Thank you for the opportunity to comment on this proposed set of requirements. I trust that my input on these rules is helpful to the agency in updating the CFR.

Sincerely,

Paul Holland

Paul V. Holland, M.D.
Medical Director/Chief Executive Officer

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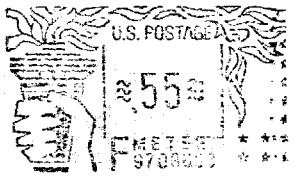

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